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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/810,434	03/15/2001	Glenn McGall	18547-042010	6484

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EXAMINER

EPPS, JANET L

ART UNIT	PAPER NUMBER
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1635

DATE MAILED: 12/17/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/810,434

Applicant(s)

GLENN MCGALL, LISA KAJISA

Examiner

Janet L. Epps

Art Unit

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-17 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-17 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

WILLIAM N. PHILLIPS
PATENT ANALYST

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DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting an essential step, such omission does not set forth the method in clear and unambiguous terms. See MPEP § 2172.01. The omitted step is a correlation, or recapitulation step at the end of the claim that restates the preamble.

Claim 2 recites the limitation "said synthesizing" in claim 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 3 (line 16), and those claims dependent thereon, claims 4-17, recite "performing additional irradiating," this phrase lacks sufficient antecedent basis since it does not appear that the recited method includes a prior step comprising "irradiating."

Claim 5 recites wherein "P is a phosphoramidite group." This phrase is vague and indefinite since the symbol "P" is generally known in the art to be the symbol for the element phosphorous.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Earhart et al. in view of McGall et al.

Earhart et al. teach a method for specifically and uniformly synthesizing oligonucleotide polymers within molecular array elements. One embodiment of the Earhart et al. invention provides a method for specifically and uniformly synthesizing desired oligonucleotides within the elements (also called cells, or features) of a molecular array. In one aspect of the present invention, a first droplet containing a specific reactive 5'-protected nucleoside phosphoramidite is applied to the surface of a molecular array substrate at a specified position. The 5'-protected nucleoside phosphoramidite reacts with hydroxyl groups on the surface of the molecular array substrate to form a single-nucleotide, nascent, substrate-bound oligonucleotide within an element with boundaries defined by the area of the surface of the molecular array substrate covered by the first droplet. After first rinsing away any unreacted 5'-protected nucleoside phosphoramidite, deactivating remaining unreacted surface hydroxyls with a capping agent solution, and finally activating the nascent, substrate-bound oligonucleotide by removing a dimethoxytrityl group protecting the 5-hydroxyl oxygen atom of the nascent substrate-bound oligonucleotide, a second droplet containing a specific 5'-protected nucleoside phosphoramidite having a covering volume is applied to the surface of a molecular array substrate at the specified position. As a result, the

5'-protected nucleoside phosphoramidite in the second droplet is added to the activated, nascent, substrate-bound oligonucleotide via a polymerization reaction. A capping agent is then applied to the molecular array substrate to deactivate any unreacted deprotected nascent substrate-bound oligonucleotide (col. 4, lines 21-67; col. 5, lines 1-15). After removal of the capping agents, the phosphite triester group is oxidized by the addition of iodine in THF, pyridine, and water to form a phosphotriester group. (col. 7, lines 1-4).

The oligonucleotides of Earhart et al. are commonly represented by strings of the upper case letters A, T, C, and G, that represent adenosine, thymidine, cytosine, and guanosine subunits within the oligonucleotide, respectively (col. 9, lines 11-18). Additionally, the methods of Earhart et al. can be applied to the synthesis of high-density arrays that provide a surface comprising up to 100,000 cells or regions containing surface bound oligonucleotide (col. 5, lines 50-61), wherein each cell has a diameter of approximately 100 microns (therefore the area of these cells would be less than about 1 cm^2 and less than about 1 mm^2).

Earhart et al. discloses the basic conditions for a method of preparing a nucleic acid array as set forth in the instant claims. However, Earhart et al. does not specifically recite wherein the concentration of iodine used in the oxidation step ranges from about 0.005M to about 0.05M, wherein the iodine concentration is about 0.02 M, or wherein the nucleotide monomers are PG group is MeNPOC and wherein P is $-\text{P}(\text{OCH}_2\text{CH}_2\text{CN})\text{N}(\text{iPr})_2$ (cyanoethyl-phosphoramidite).

First, it is noted that in general, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable

ranges by routine experimentation." See MPEP § 2144.05(II). In the instant case the general conditions of oxidation, namely wherein the oxidation occurs in the presence of a solution comprising iodine in THF, pyridine, and water, are disclosed in the prior art. Therefore Applicant's recitation of a particular range of iodine concentration used in an oxidation solution is not considered inventive since there is no evidence that the particular concentration range recited in the instant claims is critical to the claimed method.

McGall et al. describe the use of photo-removable protecting groups that are preferably used in solid phase synthesis of oligonucleotides and polypeptides and high density arrays thereof (col. 5-col 6, bridging paragraph). The protecting groups of McGall et al. are typically removed by photolysis, i.e., by irradiation (col. 8, lines 56-60). McGall et al. disclose protected nucleotide monomers useful in oligonucleotide synthesis wherein said monomers comprises 3'-O-cyanoethylphosphoramidite and 5'-O-MeNPOC protected nucleosides (see col. 20, lines 5-67).

It would have been obvious to one of ordinary skill at the time of filing to modify the method of the Earhart et al. reference with the teachings of McGall et al. in the design of the present invention, because McGall et al. provide practical teachings regarding the use of photolabile molecules in solid phase synthesis of oligonucleotides that are amenable to the synthesis of high density oligonucleotide arrays. Moreover, one of ordinary skill in the art would have been motivated to modify the teachings of Earhart et al. with the protected nucleotide monomers of McGall et al. because the photocleavable protecting groups and linkers of McGall et al. are disclosed as being stable to a variety of reagents, and can be rapidly cleaved under mild conditions, and not generate highly reactive by products (col. 1, lines 56-62).


Therefore, the invention as a whole would have been prima facie obvious at the time of filing over, Earhart et al. in view of McGall et al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L Epps whose telephone number is 703-308-8883. The examiner can normally be reached on Mondays through Friday, 9:00AM to 6:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (703)-308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-746-5143 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Janet L Epps
Examiner
Art Unit 1635
December 13, 2001


SEAN MCGARRY
PRIMARY EXAMINER